Paper No. 19

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte HIROHIDE MIWA and MASATO KINO

Appeal No. 1997-1817
Application No. 08/139,693[1]

ON BRIEF

Before ROBINSON, SPIEGEL, and SCHEINER, Administrative Patent Judges.
SPIEGEL, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 through 16. Claims 17 through 48, the only other claims pending in the application, have been withdrawn from further consideration under 37 CFR § 1.142(b) as not readable on the elected invention. Claims 1, 2 and 6 through 8 are illustrative and read as follows:

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[1] Application for patent filed October 22, 1993.

1. A method for treating a body fluid related disease in a body where a retrovirus is present in the body fluid and in cells infected by the retrovirus, comprising the steps of:

administering as a Trigger Factor, a substance that stimulates the region of proliferation control in the retrovirus in an infected cell to increase proliferation rate, shorten cell life, and cause transition from an asymptomatic period to a symptomatic period, to induce death of the infected cells,

withdrawing the body fluid,

extracorporeally processing the withdrawn body fluid to kill, inactivate, or remove the pathogenic microorganisms and preferably the infected cells present in the body fluid, and

reinfusing the process body fluid

wherein the Trigger Factor is administered either prior to or in parallel with the withdrawing and processing steps.

2. The method of claim 1 wherein the retrovirus is an HIV.

6. The method of claim 2 where the infected cell is a CD4 (positive) cell selected from the group consisting of T4 Helper lymphocytes, macrophages and dendritic cells, into which the RNA of the HIV has been transcribed and inserted as a provirus; wherein the body fluid is a fluid selected from the group consisting of blood, lymphatic fluid and cerebrospinal fluid; and wherein the Trigger Factor is a substance selected from the group consisting of a biochemical substance and a medicament.

7. The method of claim 6 where the biochemical substance stimulates the provirus in the infected cell to replicate actively, subjects the infected cell to programmed death, and promotes a transition from a latent period to the AIDS related complex (ARC) period.

8. The method of claim 7 where the biochemical substance is a substance selected from the group consisting of Tumor Necrosis Factor (TNF) and anti-Fas antibody.

The references relied on by the examiner are:

MICROBIOLOGY, INCLUDING IMMUNOLOGY AND MOLECULAR GENETICS, pp. 468 and 1212 (Davis et al., ed., 2d ed., Harper & Row, Publishers, 1979) (Microbiology).

Matsuyama et al. (Matsuyama), "Cytocidal Effect of Tumor Necrosis Factor on Cells Chronically Infected with Human Immunodeficiency Virus (HIV): Enhancement of HIV Replication," Journal of Virology, Vol. 63, No. 6, pp. 2504-09 (June 1989).

D.R. Forsdyke, "Programmed Activation of T-Lymphocytes. A Theoretical Basis for Short Term Treatment of AIDS with Azidothymidine," Medical Hypotheses, Vol. 34, pp. 24-27 (1991).

ISSUES

1. Claims 1-16 stand rejected under 35 U.S.C. § 112, first paragraph, as based on a non-enabling specification.

2. Claims 1-11 and 16 stand rejected under 35 U.S.C. § 103 as being unpatentable over Forsdyke in view of Matsuyama and appellants' "admission."

3. Claims 12-15 stand rejected under 35 U.S.C. § 103 as being unpatentable over Forsdyke in view of Matsuyama and appellants' "admission" as applied to claims 1-11 and 16 above, and further in view of Microbiology.

In reaching our decision in this appeal we have given careful consideration to the appellants' specification and claims and to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's answer (Paper No. 16, mailed May 20, 1996) for the examiner's reasoning in support of the rejections and to the appellants' brief (Paper No. 15, entered February 26, 1996) and to appellants'

reply brief (Paper No. 17, entered July 18, 1996) for the appellants' arguments thereagainst.

OPINION

1. Rejection of claims 1-16 under § 112, ¶1 as based on a nonenabling specification

According to the examiner, the specification only enables "specific 'Trigger Factors'" because, while the specification recites two specific "Trigger Factors," that "recitation fails to establish a genus of 'Trigger Factor'(s) thereby placing this genus in the skilled Artisan's possession" (answer, p. 3).[2] The examiner bases his opinion on the unpredictability of the pharmaceutical art and the failure of the specification to identify the compound class(es) which possesses the required "trigger factor" activity (answer, p. 11).

Here, as pointed out by appellants, the specification provides both a specific definition of "trigger factor" and examples thereof, i.e., TNF and anti-Fas antibody (see e.g., brief, p. 9; reply brief, p. 5; specification, p. 4, ll. 14-19 and p. 17, ll. 3-16). Moreover, the prior art suggests that other "trigger factors" are known. For example, Forsdyke discusses activation of HIV-bearing T-cells as part of a polyclonal homeostatic response to "a lectin-like factor (lymphokine, growth factor)" (p. 26, col. 1,

[2]The examiner cited "MPEP §§ 706.03(n) and 706.03(z)" (answer, p. 3). These sections are entitled "Correspondence of Claim and Disclosure" and "Undue Breadth," respectively, and last appeared in the Sixth Edition of the MPEP (Jan. 1990). See Rev. 1 of the Sixth Edition of the MPEP (Sept. 1995). We observe that both of these sections remained unchanged since at least Rev. 6 of the Fifth Edition of the MPEP (Oct. 1987). Neither section refers to 35 U.S.C. § 112, first paragraph, in whole or by requirement, and thus we will not further refer in this decision to either of these MPEP sections.

para. 3) and suggests that TNF is also a suitable polyclonal growth factor (p. 26, col. 2, para. 2); and, Matsuyama identifies several factors reported to activate HIV gene expression, including granulocyte-macrophage colony stimulating-factor, immunological stimuli, infection with viruses such as herpes simplex virus type 1, 12-*O*-tetradecanolyphorbol-13-acetate and lymphotoxin (p. 2504, col. 1, para. 1-2) and TNF (p. 2507, col. 1, para. 3).

A specification of a patent application is presumed to comply with the enablement requirement of 35 U.S.C. 112, first paragraph. An examiner may reject claims in a patent application on the basis of an alleged failure of the applicant to comply with the enablement requirement if the examiner can establish by a preponderance of the evidence that there is reason to doubt the objective truth of the statements contained in the specification. In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1970). In our opinion, the examiner has not sustained his burden for making the enablement rejection, relying instead on mere conclusory statements. Moreover, it appears inconsistent to assert that the claimed invention is only enabled for "specific 'Trigger Factors'" (answer, p. 3), presumably TNF and anti-Fas antibody, as recited in claim 8 and then to conclude that claim 8 is not enabled. The examiner argues that while "[a]pplicants' claims read on TNF from any source," "TNF does not possess species cross over; that being mouse TNF fails to provide a physiological effect in humans, with mouse TNF not effecting [sic, affecting] humans"

(answer, p. 11). However, the examiner has failed to explain how the lack of species crossover would have amounted to undue experimentation for the skilled artisan given appellants' specification and knowledge generally available to those skilled in the art.

Therefore, the rejection under 35 U.S.C. § 112, first paragraph, is reversed.

2. Rejection of claims 1-11 and 16 under § 103 over Forsdyke, Matsuyma and appellants' "admission"

The examiner bears the initial burden of establishing a prima facie case of obviousness. To establish a prima facie case of obviousness, there must be both some suggestion or motivation to modify the reference or combine reference teachings and a reasonable expectation of success. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). It is insufficient that the prior art discloses the components of the claimed invention, either separately or in other combinations; there must be some teaching, suggestion, or incentive to make the combination made by appellants. Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1988) (insufficient to select from the prior art the separate components of the inventor's combination, using the blueprint supplied by the inventor).

Forsdyke discloses that effective therapy of AIDS requires achieving two results, i.e, "activation of all host cells carrying latent virus so that such cells will be destroyed by the virus. ... [and] prevention of liberated viruses infecting, replicating in and establishing latency in previously uninfected cells" (p. 25, col. 2, para. 3). According to Forsdyke, host cells activation occurs under two circumstances, i.e., upon a random

chance encounter of the infected person with a particular antigenic determinant (monoclonal response) or as part of a polyclonal response to a lectin-like factor (lymphokine, growth factor) (p. 26, col. 1, para. 3).

> Currently, treatment with AZT must be prolonged because the triggering of latent HIV DNA to destroy itself is mainly dependent on G0/G1 switches generated by random antigenic signals. ... However, if all host T-lymphocyte were activated synchronously by an appropriate concentration of an appropriate growth factor, all the integrated HIV DNA molecules would be destroyed with their host cells. Furthermore, all liberated RNA viruses could be prevented from replicating in previously uninfected cells by a short and intensive concomitant course of AZT. [Page 26, para. bridging cols. 1-2.]

Forsdyke explicitly references Matsuyama[3] as suggesting that TNF is a suitable polyclonal growth factor for activating latent HIV (abstract; p. 26, col. 2, para. 2).

Matsuyama discloses that TNF preferentially kills HIV-infected cells and enhances HIV-replication (p. 2507).

According to the examiner, appellants have allegedly admitted on page 11 of the specification that "[n]ew methods of extracorporeal blood processing by the inventors are presented as shown below; however, the extracorporeal blood processing can be prior art" (answer, para. bridging pp. 4-5).

The examiner's position, as best it is understood, is that the in vitro elimination of HIV-infected cells by Matsuyama is constructively an extracorporeal processing step (answer, p. 17, first full para.). Thus, it would have been obvious to use a conventional

[3]Footnote 33 in Forsdyke identifies Matsuyama et al. as the same Matsuyama relied upon by the examiner as prior art in this rejection.

therapeutic administration route, e.g., extracorporeal processing, to treat HIV-infected cells with AZT/TNF as suggested by Forsdyke and Matsuyama (answer, p. 15).

In our opinion, with or without appellants' alleged admission,[4] the examiner has not provided the requisite motivation or suggestion to combine the AZT/TNF HIV-treatment of Forsdyke and Matsuyama with known extracorporeal blood processing methods for treating retroviral infections as claimed. Neither Forsdyke nor the in vitro procedure of Matsuyama discloses or suggests "reinfusing the process body fluid" as required by claim 1 and its dependent claims. The examiner has not explained why one of ordinary skill in the art would have reasonably considered a process performed in a test tube, i.e., Matsuyama's in vitro experiment for infected cells in bovine serum, as equivalent to or a substitute for extracorporeal processing of a body fluid as recited in claim 1.

Based on this record, we find that the examiner has relied on impermissible hindsight in making his determination of obviousness. In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992) (“It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant’s structure as a template and selecting elements from references to fill the gaps”).

[4]According to appellants, "[r]ather than an admission, the Appellants have simply stated that the extracorporeal processing that will be employed in the invention, can be accomplished by their proposed new method and by other such extracorporeal processing methods that presently exist. ... The mere existence of a technique does not make its use obvious." (brief, para. bridging pp. 12-13); and, "Appellants [sic] alleged 'admission' is simply an acknowledgment [sic] that some methods of extracorporeal blood processing exist." (brief, para. bridging pp. 15-16).

Accordingly, the rejection of claims 1-11 and 16 rejected under 35 U.S.C. § 103 as being unpatentable over Forsdyke, Matsuyama and appellants' "admission" is reversed.

3. Vacatur of the rejection of claims 12-15 under § 103 over Forsdyke, Matsuyama, appellants' "admission" and Microbiology

Our consideration of this rejection leads us to conclude that it is not in condition for a decision on appeal. According to the answer (pp. 2-3, § (7) Prior Art of Record), the examiner is relying on pp. 468 and 1212 of Microbiology. However, the examiner refers to pages 648 and 1212 of Microbiology in his rejection of claims 12-15 (answer, p. 5). The record copy of Microbiology only contains pages 468 and 1212. Thus, it is unclear what portion of Microbiology the examiner is relying on for what disclosure. It is impossible to tell whether or not the disclosure in Microbiology remedies the deficiency in the combination of Forsdyke and Matsuyama, with or without appellants' "admission." Therefore, we vacate the rejection of claims 12-15 under § 103 over Forsdyke, Matsuyama, appellants' "admission" and Microbiology; and, remand the application to the examiner to clarify the basis of rejection and to take appropriate action.

OTHER ISSUES

Upon return of this application to the jurisdiction of the examiner, the examiner should take a step back and re-evaluate the disclosure of Forsdyke in combination with the disclosure in Kroyer (US Patent 4,908,014, issued March 13, 1990), discussed in appellants' specification as reference (*m) and submitted in the Information Disclosure

Statement entered February 14, 1994 (Paper No. 4). We note that Kroyer discusses extracorporeal processing of body fluids to kill viruses, e.g., HIV, and undesired cells therein, using heat and, optionally, adding virus-attenuating pharmaceuticals to the fluid while it is in the extracorporeal device and/or exposing the fluid in the device to UV light, etc.

In the event of any further action by the examiner, we urge the examiner to structure his § 103 rejection consistent with the inquiries that are required for establishing a factual basis to support a legal conclusion of obviousness as set forth in Graham v. John Deere Co., 383 U.S. 1 , 17, 148 USPQ 459, 467 (1966), e.g., using the model set forth in Section 706.02(j) of the Manual of Patent Examining Procedure (MPEP) as follows:

> the examiner should set forth ... (1) the relevant teachings of the prior art relied upon, preferably with reference to the relevant column or page number(s) and line number(s), where appropriate, (2) the difference or differences in the claim over the applied reference(s), (3) the proposed modification of the applied reference(s) necessary to arrive at the claimed subject matter, and (4) an explanation why such proposed modification would have been obvious to one of ordinary skill in the art at the time the invention was made.

Adherence to this model will ensure that the examiner considers the claims individually and that the statement of the rejection will clearly and concisely apply the relevant evidence of obviousness to the subject matter of an individual claim.

CONCLUSION

In conclusion, the decision of the examiner (1) to reject claims 1-16 under 35 U.S.C. § 112, first paragraph, as based on a non-enabling specification is reversed, (2) to reject claims 1-11 and 16 under 35 U.S.C. § 103 as being unpatentable over Forsdyke in view of Matsuyama and appellants' "admission" is reversed and (3) to reject claims 12-15 under 35 U.S.C. § 103 as being unpatentable over Forsdyke in view of Matsuyama and appellants' "admission" as applied to claims 1-11 and 16 above, and further in view of Microbiology is vacated.

REVERSED-IN-PART; VACATED-IN-PART

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